**UNITED STATES PATENT AND TRADEMARK OFFICE**

---

**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

---

*Ex parte* SAMY ASHKAR and JAIRO SALCEDO

---

Appeal 2007-1623
Application 09/981,845
Technology Center 1600

---

Decided: September 14, 2007

---

Before ERIC GRIMES, NANCY J. LINCK, and
RICHARD M. LEBOVITZ, *Administrative Patent Judges.*

GRIMES, *Administrative Patent Judge.*

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 involving claims to peptides. The Examiner has rejected the claims as nonenabled. We have jurisdiction under 35 U.S.C. § 6(b). We affirm in part.

BACKGROUND

"The primary challenges faced in the fabrication of new endosseous implants are to increase the rate of osseointegration and the percentage of bone apposition. . . . The interaction between the titanium oxide layer of

dental implants and certain extracellular matrix proteins may be a prerequisite for reproducible direct apposition of bone to titanium implants." (Specification 1: 17-31.)

The Specification discloses that osteopontin (OPN) binds to integrin-type receptors and influences a wide range of biological processes (*id.* at 1: 32 to 2: 10). "[T]he RGD sequence [in osteopontin] appears to mediate cell attachment via integrin receptors and thereby activate signal transduction pathways with[in] the cell. Cleavage of osteopontin by thrombin has been reported to enhance the ability of cells to attach and spread *in vitro* . . . , suggesting that thrombin cleavage makes the RGD motif more accessible." (*Id.* at 2: 11-16.)

"[T]he naturally occurring human osteopontin secreted from human osteoblast cells" is disclosed to have the amino acid sequence shown in SEQ ID NO: 1 (*id.* at 11: 5-6). SEQ ID NO: 1 is 314 amino acids in length. The Specification discloses several smaller, osteopontin-related peptides, including the one having the amino acid sequence shown in SEQ ID NO: 11 (*id.* at 12: 3-19). SEQ ID NO: 11 has the following sequence: RSRRATEV FTPVVPTVDTYDGRGDSVVYGRRSKSKKFRRPAGAAGGPAGPAGPA GPAGPAGPA (*id.* at 12: 9-10). The underlined amino acids are part of the amino acid sequence of SEQ ID NO: 1 (amino acids 142 to 177); i.e., they are a part of osteopontin. The amino acids before and after the underlined amino acids are not part of osteopontin.

The Specification provides a working example that describes the attachment and spreading behavior of osteoprogenitor cells on plates coated with SEQ ID NO: 11 and SEQ ID NO: 15 (*id.* at 53-55). (SEQ ID NO: 15 is

an acetylated peptide that is the same as SEQ ID NO: 11 except that it lacks the C-terminal non-osteopontin amino acids.) The example shows that SEQ ID NO: 11 and SEQ ID NO: 15 both promote the attachment and spreading of osteoprogenitor cells, and that the activity of SEQ ID NO: 15 was inhibited by antibodies to the $\alpha_v\beta3$ receptor but was not inhibited by antibodies to the CD44 or $\alpha\beta1$ receptors (*id.* at 54-55, Table 8).

DISCUSSION

1. CLAIMS

Claims 1-3, 5, and 6 are on appeal and read as follows:

1. An active ostopontin peptide fragment comprising an amino acid sequence selected from the group consisting of SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, and SEQ ID NO:15, wherein the peptide binds to at least one integrin receptor on a cell surface selected from the group consisting of $\alpha v\beta3$, $\alpha v\beta5$, $4\beta1$, $2\beta1$, VCAM, ICAM CD44, V3Vx.

2. The peptide fragment of claim 1, wherein the peptide increases cell attachment to a biomaterial and increases cell spread.

3. The peptide fragment of claim 1, wherein the peptide binds to at least one integrin receptor on a cell surface selected from the group consisting of VCAM, ICAM CD44, and V3Vx.

5. The peptide fragment of claim 1 wherein the integrin(s) is selected from the group consisting of $\alpha v\beta3$, $\alpha v\beta5$, $4\beta1$, and $2\beta1$.

6. The peptide fragment of claim 1 wherein the cell is selected from the group consisting of osteoprogenitor cells, tumor cells, macrophages, periosteal cells, endothelial cells, epithelial cells, eosinophils, stem cells, limited potential precursor cells, precursor cells, committed precursor cells, and differentiated cells.

The Examiner made an election-of-species requirement (Office action mailed March 6, 2003) and Appellants elected the species of SEQ ID NO: 11 (Paper received April 7, 2003). Thus, up to this point, only the claimed embodiment of SEQ ID NO: 11 has been examined on the merits.

2. PRIOR ART

The Examiner relies on the following references:

Hu et al., "A biochemical characterization of the binding of osteopontin to integrins $\alpha_V\beta_1$ and $\alpha_V\beta_5$," J. Biol. Chem., Vol. 270, No. 44, pp. 26232-26238 (1995).

Tuck et al., "Osteopontin-induced, integrin-dependent migration of human mammary epithelial cells involves activation of the hepatocytes growth factor receptor (Met)," J. Cell. Biochem., Vol. 78, pp. 465-475 (2000).

3. ENABLEMENT

Claims 1-3, 5, and 6 stand rejected under 35 U.S.C. § 112, first paragraph, as not enabled throughout their full scope. The Examiner acknowledges that the Specification is enabling for a peptide comprising SEQ ID NO: 11 that binds to the αvβ3 integrin receptor and increases attachment and spreading of osteoprogenitor cells (Answer 3) but concludes that the Specification does not enable those skilled in the art to use SEQ ID NO: 11 to bind to any of the other receptors listed in claim 1 or to promote attachment and spreading of the other types of cells listed in claim 6 (*id.* at 3-4). The Examiner cites references teaching that osteopontin "binds integrin receptors $\alpha_v\beta_3$, $\alpha_v\beta_1$ and $\alpha_v\beta_5$, not all the integrins as recited in instant claim 1" and that osteopontin binds the $\alpha_v\beta_3$ receptor in some cell lines but not in others (*id.* at 5). The Examiner concludes:

> It would require an indeterminate quantity of unpredictable investigational experimentation of the skilled artisan to determine which integrin receptor bound the claimed osteopontin peptide fragments, then discern which cell type expressed that specific receptor and if that cell type was conducive to osseointegration activity. Without sufficient guidance, the amount of experimentation would be undue for one skilled in this art. Thus only osteoprogenitor cells and αvβ3 integrin receptors meet the limitations of the instant claims.

(*Id.* at 5-6.)

Appellants argue that "[i]t is well known in the art that osteopontin binds to more than one integrin receptor" (Br. 7, citing Hu), and that "SEQ ID NO 11 and 15 have conserved domains similar to osteopontin. One of ordinary skill in the art would expect the claimed peptides to bind to receptors capable of binding osteopontin" (*id.*). Appellants also argue that the

> ability of the peptides recited in claim 1 to bind to *at least one* integrin receptor on the cell surface is in fact demonstrated by the ability of anti-integrin antibodies to inhibit cell attachment. . . . There is no legal requirement that the claimed peptides bind all integrins or to all cell types for the peptides to have the specified utility. . . . As long as the specification discloses at least one method for making and using the claimed invention that bears a reasonable correlation to the entire scope of the claim, then the enablement requirement of 35 U.S.C. 112 is satisfied.

(*Id.* at 7-8.)

We agree with Appellants that the Examiner has not adequately shown that practicing the claimed method would require undue experimentation. "[T]he question of undue experimentation is a matter of degree. The fact that some experimentation is necessary does not preclude

enablement; what is required is that the amount of experimentation 'must not be unduly extensive.'" *PPG Indus. Inc. v. Guardian Indus. Corp.*, 75 F.3d 1558, 1564 (Fed. Cir. 1996).

Here, the claims only require that the claimed peptide interact with at least one of the listed receptors. The Specification shows that SEQ ID NO: 11 and SEQ ID NO: 15 share the same osteopontin subsequence, and that antibodies to the $\alpha_v\beta_3$ receptor block the cell attachment and cell spreading activity of SEQ ID NO: 15. Based on these data, it is reasonable to conclude that SEQ ID NO: 15 binds to the $\alpha_v\beta_3$ receptor and, based on structural similarity, it is reasonable to expect that SEQ ID NO: 11 does, too. Thus, the evidence is adequate to show that the peptide having the amino acid sequence shown in SEQ ID NO: 11 binds to at least one of the integrin receptors recited in claim 1. No more is required to enable claim 1 (to the extent it has been examined following the election-of-species requirement).

Similarly, claim 6 only requires that the peptide promote attachment and spread of one of the listed types of cells. The Specification discloses that the peptide of SEQ ID NO: 11 promotes attachment and spreading of osteoprogenitor cells, which is one of the listed types of cells. Again, that is all the claim requires with respect to SEQ ID NO: 11. As long as the full scope of the claim is enabled by the disclosure, a patent application need only disclose one method of making and using a claimed invention in order to satisfy the enablement requirement. *See Johns Hopkins Univ. v. Cellpro Inc.*, 152 F.3d 1342, 1361 (Fed. Cir. 1998) ("The enablement requirement is met if the description enables any mode of making and using the invention.").

In summary, the Examiner has not asserted that the Specification does not enable those skilled in the art to *make* peptides comprising SEQ ID NO: 11, and the Specification appears to enable a person skilled in the art to *use* the peptide of SEQ ID NO: 11 to promote attachment and spreading of osteoprogenitor cells via its interaction with the $\alpha_v\beta_3$ receptor. We therefore reverse the rejection of claims 1, 2, 5, and 6.

However, we affirm the rejection of claim 3. The evidence of record does not provide an adequate basis on which to conclude that the peptide of SEQ ID NO: 11 is likely to bind to any of the receptors recited in claim 3. The results shown in the Specification's Table 8 (pages 54-55), in fact, show that antibodies to the CD44 receptor do not affect the cell attachment and cell spreading activity of SEQ ID NO: 15. Based on those results, those skilled in the art would expect that the peptides of SEQ ID NO: 15 and SEQ ID NO: 11 does *not* bind to the CD44 receptor.

The Specification provides no other persuasive evidence that the osteopontin subsequence shared by SEQ ID NO: 11 and SEQ ID NO: 15 interacts with any of the receptors listed in claim 3. Therefore, we agree with the Examiner that, with respect to the embodiment of the claims that is directed to the peptide of SEQ ID NO: 11, undue experimentation would be required to make and use peptides comprising SEQ ID NO: 11 that bind to at least one of the receptors listed in claim 3.

OTHER ISSUES

On return of this application, the Examiner should consider whether the scope of the claims is reasonably definite. Specifically, the preamble of the claim recites an "active osteopontin peptide fragment." The

Specification defines "active osteopontin peptide" to mean a fragment of osteopontin (Specification 11: 9-11). The peptide of SEQ ID NO: 11, however, is not a fragment of OPN because it includes non-OPN sequences. The Examiner should consider whether the effect of the preamble, read in light of the Specification, on the scope of the claims is sufficiently definite to pass muster under 35 U.S.C. § 112, second paragraph.

Also, "[t]he cell" in claim 6 lacks antecedent support in claim 1, from which claim 6 depends.

SUMMARY

We reverse the rejection under 35 U.S.C. § 112, first paragraph, of claims 1, 2, 5, and 6, but affirm the rejection of claim 3.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a).

AFFIRMED IN PART

lbg

PATREA L. PABST
PABST PATENT GROUP LLP
400 COLONY SQUARE, SUITE 1200
1201 PEACHTREE STREET
ATLANTA GA 30361